Anti-Keratin Antibodies in Human Sera: Naturally Occurring or Induced?

To the Editor:

The report by Iwatsuki and colleagues [1] on the specificty of antiepidermal antibodies to keratins suggested it might be useful to note briefly our observations of antikeratin antibodies (AKA) and their immunofluorescent (IF) staining patterns, and to assess the clinical significance of AKA.

Epidermal cytoplasmic antibodies reactive with the basal cells (B-Cyt-Abs) of mouse and rat esophagus were initially observed by indirect IF in the sera of 13 of 27 (48%) acute and convalescent burn patients at titers of 1:10–1:40 [2]. The IF staining pattern of these antibodies were as illustrated by Iwatsuki and colleagues [1] in their Fig 1*D*. Subsequent studies, including human skin as a substrate, and a review of the frequency of B-Cyt-Abs, disclosed an incidence of 11% (22 of 207) [3]. The possible pathognomonic significance of B-Cyt-Abs, other than that considered by Iwatsuki et al [1], has been considered in brief in an earlier communication to the *Journal* [4], as well as in detail elsewhere [3].

Our other initial observation of AKA, in this case to AKA referred to as the granular type (the other types being laminar and diffuse) [5], came during the study of the specificity of antiepithelial antibodies in the sera of patients with benign prostatic hypertrophy (BPH) and prostate cancer (PCa) [6]. In a subsequent follow-up study of patients with prostatic disease, AKA of the laminar type (which appear similar to that of the IF staining pattern identified in Fig 1*B* by Iwatsuki et al [1] as being reactive with the upper layer (U-Cyt)) have been seen in 7 of 42 (17%) BPH patients at titers from 1:10–1:40 and in 6 (25%) PCa patients at tiers from 1:10–1:160 [7].

As reviewed by Iwatsuki et al [1], AKA occur under a variety of clinical circumstances, including even in "normal" individuals, and as such are certainly not pathognomonic. However, the possible commonality of origin and/or cross-reactivity of AKA with keratin-like proteins of eptihelial cells, as suggested [1], in addition to other explanations for their presence [2,3,6], remains to be delineated.

In the interim, it perhaps would behoove us to note that based on the earlier reports by Young et al [8] and Youinou et al [9], high titers of AKA have heretofore mainly been thought of: (1) as being restricted to patients with connective tissue disease, principally rheumatoid arthritis, and (2) as a means to differentiate rheumatoid arthritis from other diseases of connective tissue origin. However, the observations by Iwatsuki et al [1], together with those of our earlier and recent studies, suggest that as the occurrence of AKA is much more common than previously thought, their clinical significance, particularly with respect to connective tissue disease, may require reevaluation. It may be noted, however, that the presence of AKA may be a caveat in view of the earlier suggested association between prostatitis and Reiter's syndrome, anklosing spondylitis, and uveitis [10].

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REPLY

We are pleased that R. J. Ablin confirms our demonstrations on antikeratin antibodies (AKA) in human sera.

It is now clearly established that AKA occur as natural antibodies in most animal and human sera as reported by several authors and very recently by Serre et al [1]. Such antibodies with high titers are detectable by indirect immunofluorescence in various pathologic conditions, mainly in rheumatoid arthritis.

However these findings raise many questions: We may suppose that AKA may be induced by the liberation of autoantigenic material normally hidden to the immune system by its intracellular location, as recently suggested by Grubauer et al [2]; however, the precise role of AKA in such conditions is unknown. It has been suggested that IgG antikeratin intermediate filaments may serve as opsonins to enhance the phagocytosis of keratin aggregates after cell death by monocytes and polymorphonuclear cells [2]. However the function of AKA IgM, either to remove damaged cellular components or to play a role in self-tolerance by acting as blocking antibodies, is not yet well established. It is also possible that AKA could arise in vivo from polyclonal lymphocyte activation as shown by in vitro studies. The production of anti-intermediate filament antibodies by human B lymphocytes (either with the hybridoma technology or by the transformation of B cells using Epstein-Barr virus) [3,4] may represent a common feature of the normal B-cell repertoire of the host. In autoimmune diseases the hypothesis that AKA might be the consequence of the immune system dysfunctions remains to be demonstrated.

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